IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Gleave, et al. Application No.: ~~09/967,726~~ copy filed in 09/913,325 Filed: 9/28/2001 Title: Chemo-and Radiation-sensitization of Cancer by Antisense TRPM-2 Oligodeoxynucleotides Attorney Docket No.: UBC.P-022 Customer No.: 021121	Group Art Unit: 1635 Examiner: Tracy Ann Vivlemore Confirmation No: 6881

Commissioner for Patents

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DECLARATION UNDER RULE 132

The undersigned each hereby declare as follows:

1. I am a named inventor of the above-captioned application. As such, I am familiar with the application, including the claims.

2. This declaration is submitted to set forth results from clinical trials that have been conducted since the filing of the application.

3. This declaration is signed by less than all of the inventors, because the other inventors, H. Miyake and T Zellweger, are no longer associated with the project, and have had no involvement, and thus no personal knowledge of the trials reported here.

4. Limited clinical testing (two Phase I studies) has been conducted to evaluate toxicity of OGX-011, an antisense oligonucleotide that has the sequence as set forth in Seq. ID NO.: 4 of the above-captioned application. The oligonucleotide is modified as described in Application Serial No. 10/080,794. A total of 25 patients with localized prostate cancer with high risk features were enrolled in the first study. In the second study, a total of 30 patients suffering from renal cancer, non-small cell lung cancer, ovarian cancer, peritoneal cancer or prostate cancer were enrolled, each of whom was refractory to one or more prior treatment regimens.

5. In both phase I studies, antisense treatments were made at levels of 40, 80, 160, 320, 480 or 640 mg and administered intravenously 3 times during the first week, and once a week thereafter. In the first phase I study, antisense therapy was combined with concurrent hormone ablation therapy for 5 weeks prior to radical prostatectomy. Concentrations of OGX-011 in prostate tissue and of TRPM-2 mRNA and protein in prostate and lymph node tissue were determined. At all levels of antisense, dose-dependent reduction in levels of TRPM-2 mRNA was observed in the lymph nodes of the patients treated, and in laser captured, micro-dissected prostate cancer levels, indicating that all of the amounts of antisense tested had a measurable affect at the expression level. The amount of TRPM-2 in serum also decreased in a dose-dependent manner.

6. This study established a dose of 640 mg as the recommended dose based on safety, tolerability, and tissue levels of antisense and TRPM-2 mRNA and/or protein.

7. In the second Phase I study, two schedules of concurrent docetaxel treatment were evaluated: 30 mg/m^2 weekly or 75 mg/m^2 every three weeks. Of 18 patients with measurable disease, the interim response rate (the study is still in progress) was 38.9%, including 33.3% with stable disease, and 5.6% achieving an objective partial response.

8. Two ovarian cancer patients showed reductions in the measured amount of the tumor marker CA125. In one patient receiving 160 mg OGX-011, the amount of CA125 marker decreased from 19,600 to 4720 over 71 days after commencement of treatment. In another who received 480 mg OGX-011, the marker level decreased from 2000 before treatment to around five hundred after 33-44 days. A slight increase to around 900 was observed during a second treatment cycle. Other patients with ovarian cancer had low initial CA125 and so a decrease could not be evaluated.

9. Two prostate cancer patients showed reduction in the amount of PSA tumor marker. In one patient receiving 40 mg OGX-011, the PSA level decreased from 90 prior to therapy to 35 after 4 treatment cycles at approximately 45 day intervals, and remained at 56 at a later date. In a second patient receiving 320 mg OGX-011, the PSA level dropped from a pre-treatment level of 1478 to a level of about 425 after 4 cycles of treatment.

10. The selection of initial dosages for this study was consistent with standard protocols for clinical trials to evaluate toxicity, and no experimentation was needed to arrive at dosage levels that produced observable reduction in TRPM-2 mRNA or serum TRPM-2.

11. While the data in this study is preliminary and difficult to draw many conclusions from because of the small sample size, the number of variables that were considered, including prior treatment of the patients, and the short duration of the test, several conclusions can be drawn. Standard

protocols for trial design were used and arrived, without experimentation, at working levels for antisense dosing that produced reduction in TRPM-2 mRNA and serum TRPM-2 without significant toxicity, and this treatment in combination with docetaxel produced beneficial results in patients who had been refractory to prior treatment.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

dated: April 6/05

Martin Gleave

dated: April 5/05

Paul Rennie

dated: April 5/05

Colleen Nelson